Introduction to charged particle therapy

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Overview

- Introduction
- Physics of ion radiotherapy
- Biological aspects
- Accelerators and gantries
- Historical Background
- Conclusions

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Introduction

Cancer

Second leading cause of death

8.8 million deaths in 2015

Nearly 1 in 6 deaths is due to cancer

The number of new cancer cases per year is expected to rise to 23.6 million by 2030

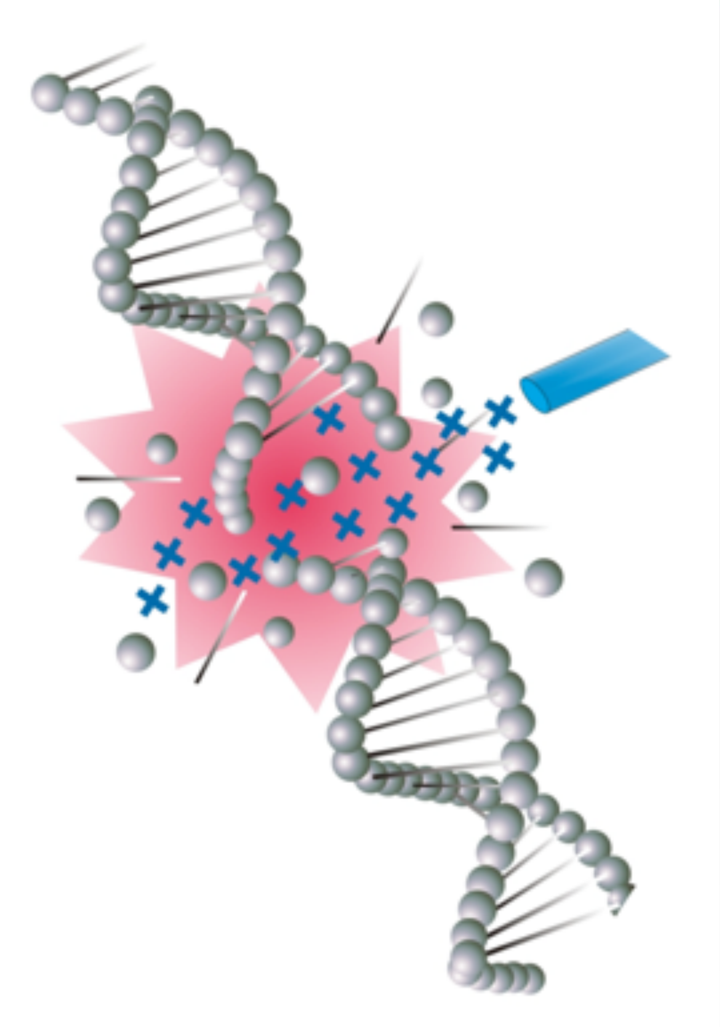
World Health Organization

~50%

of patients suffering cancer treated with radiotherapy as a stand alone or in association with other therapies

Radiotherapy

- Precisely targeted high-energy rays kill cancer cells by damaging cellular DNA
- Conventional RT performed using high energetic x-ray beams



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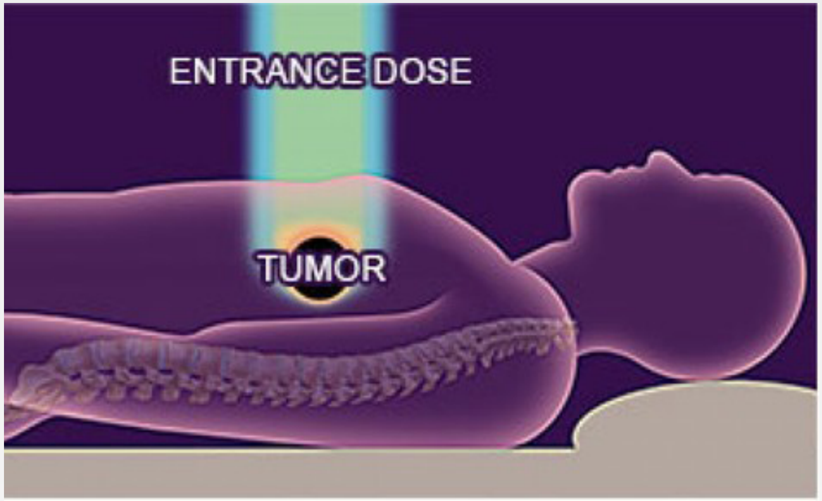
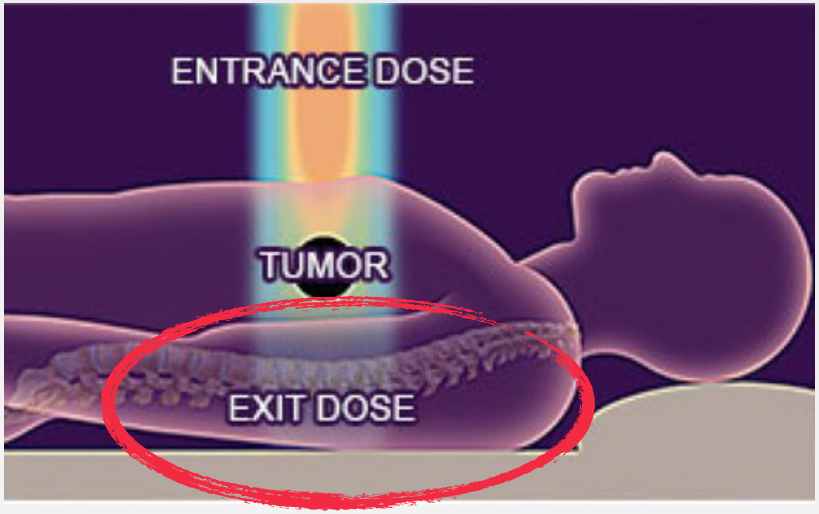
100 % of dose needed to kill the cancer cells deposited over the Planned Target Volume (PTV)

0% of dose received by surrounding Organs At Risk(OARs)

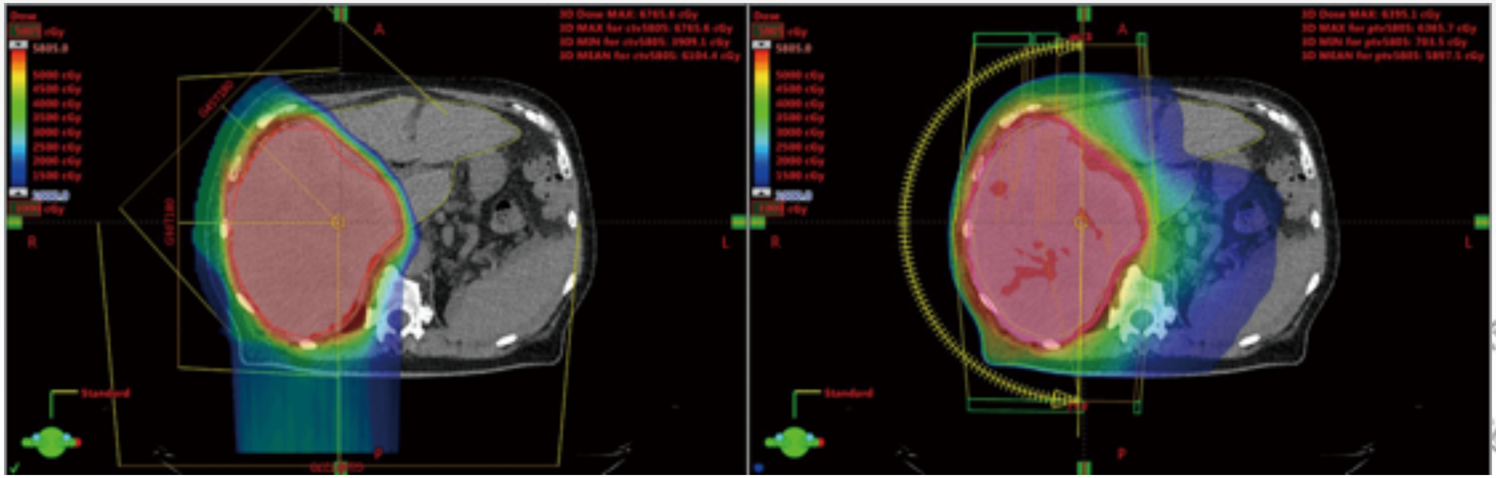
Why use ions for cancer treatments?



Charged particle therapy



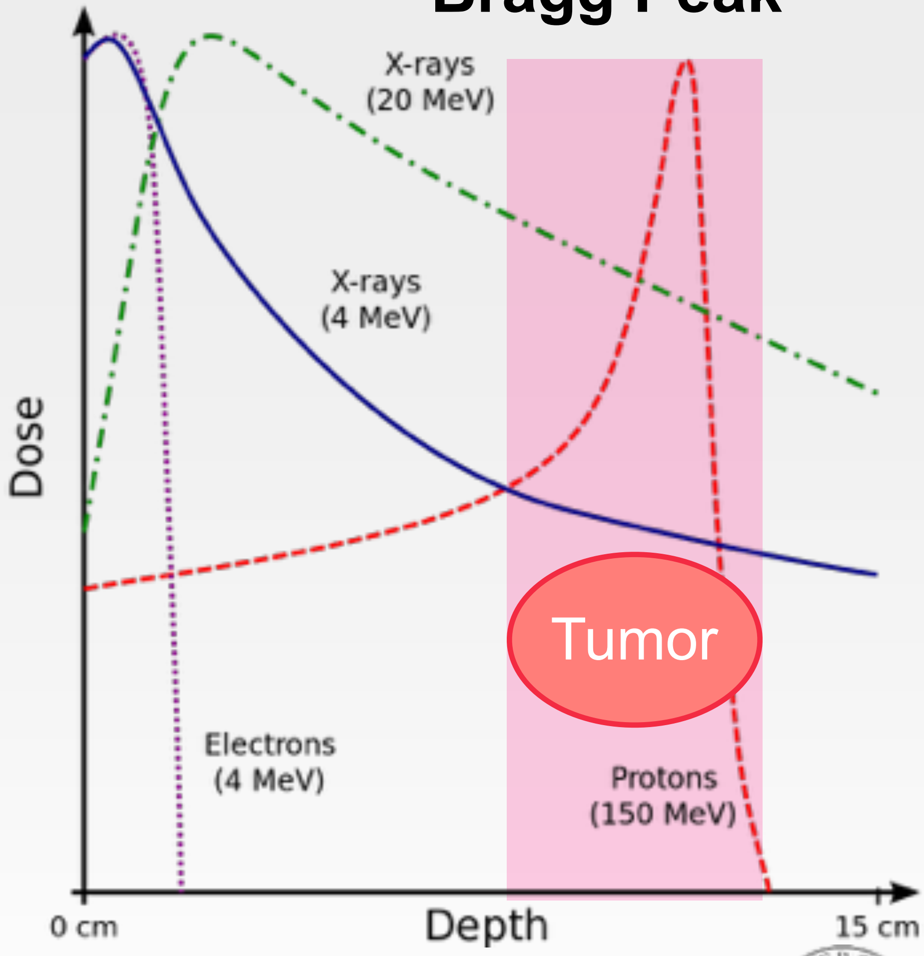
Photon therapy



Physics of ion radiotherapy

- Energy deposition focused at a specific depth (particle range) depending on the initial energy
- High Ratio Peak/Plateau
- The beam stops in the tumor, no exit dose

Bragg Peak



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Physical quantities

Fluence

$$\Phi = \frac{dN}{da}[m^{-2}]$$

Physical dose

$$D = \frac{d\epsilon}{dm}[1Gy = 1J/kg]$$

Water is used as tissue reference medium.

For a parallel beam with particle fluence Φ the dose deposited in a thin slice of an absorber material with mass density can be calculated as follows:

$$D[\mathrm{Gy}] = 1.6 \times 10^{-}9 \times \frac{dE}{dx}\left[\frac{\mathrm{keV}}{\mu\mathrm{m}}\right] \times \Phi[\mathrm{cm}^{-2}] \times \frac{1}{\rho}\left[\frac{\mathrm{cm}^3}{\mathrm{g}}\right]$$

Stopping of high energy ions

Bethe-Bloch equation in relativistic version *Fano, 1963*

$$\frac{dE}{dx} = \frac{4\pi e^2 Z_t Z_p^2}{m_e v^2}\left[ln\frac{2m_e v^2}{\langle I\rangle} - ln(1-\beta^2) - \beta^2 - \frac{C}{Z_t} - \frac{\delta}{2}\right]$$

Z_p, Z_t : nuclear charges of projectile and target

m_e, e : electron mass and charge

$\langle I\rangle$: mean ionization energy

$\frac{C}{Z_t}$: shell correction term

$\frac{\delta}{2}$: density correction term

Wilson, 1946

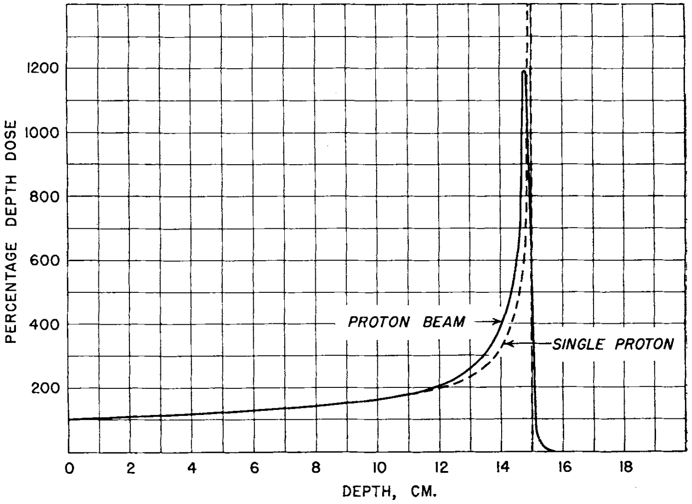

Fig. 2. The dotted curve shows the relative dose due to a single 140 Mev proton. The full curve shows qualitatively the depth dose curve for a beam of 140 Mev protons in tissue.

The maximum energy-loss rate, corresponding to the Bragg peak, is reached at a projectile velocity of:

$$v_p \approx= \frac{Z_p^{2/3}}{v_0}$$

$$v_0 = \frac{e^2}{\hbar}$$: Bohr velocity corresponding to

$$\beta = \frac{e^2}{\hbar c} = \frac{1}{137}$$

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Range

The total path length of the particle’s trajectory in the absorber

$$R(E) = \int_0^E \left(\frac{dE'}{dx}\right)^{-1} dE'$$

Statistical fluctuations of the energy loss in the large number of collisions of the slowing-down process result in a broadening of the Bragg peak for an ion beam consisting of many particles *(Vavilov, 1957)*.
The distribution of these fluctuations in the limit of many collisions becomes a Gaussian

$$f(\Delta E) = \frac{1}{\sqrt{2\pi\sigma_E}} \exp \frac{(\Delta E - \overline{\Delta E})^2}{2\sigma_E^2} \qquad \sigma_E = 4\pi Z_p Z_t e^4 N \Delta x \left[\frac{1-\beta^2/2}{1-\beta^2}\right]$$

The variance of the range staging is dependent from the variance of the energy straggling

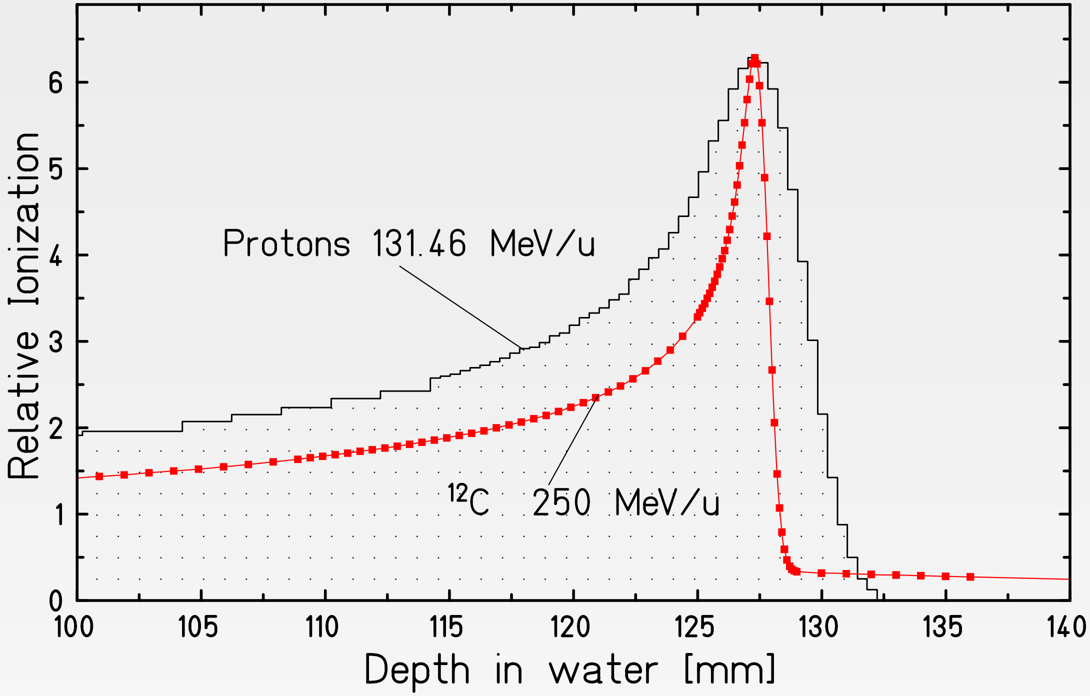
$$\sigma_R^2 = \int_0^E \left(\frac{d\sigma_E}{dx}\right)\left(\frac{dE}{dx}\right)^{-3} dE$$

The ratio of the straggling width and mean range is nearly constant and can be described by

$$\frac{\sigma_R}{R} = \frac{1}{\sqrt{M}} f\left(\frac{E}{Mc^2}\right)$$

f : slowly varying function depending on the absorber *(Rossi, 1952)*
E and *M:* particle energy and mass

Straggling comparison for p and heavier ions



The relative straggling it is smaller for heavier ions than for protons, e.g., a factor of 3.5 for ^{12}C ions.

The profile of the Bragg peaks is broader, mainly due to the density inhomogeneities of the penetrated tissue

Characteristic dose tail behind the Bragg peak, which is caused by secondary **fragments** produced in nuclear reactions along the stopping path of the ions

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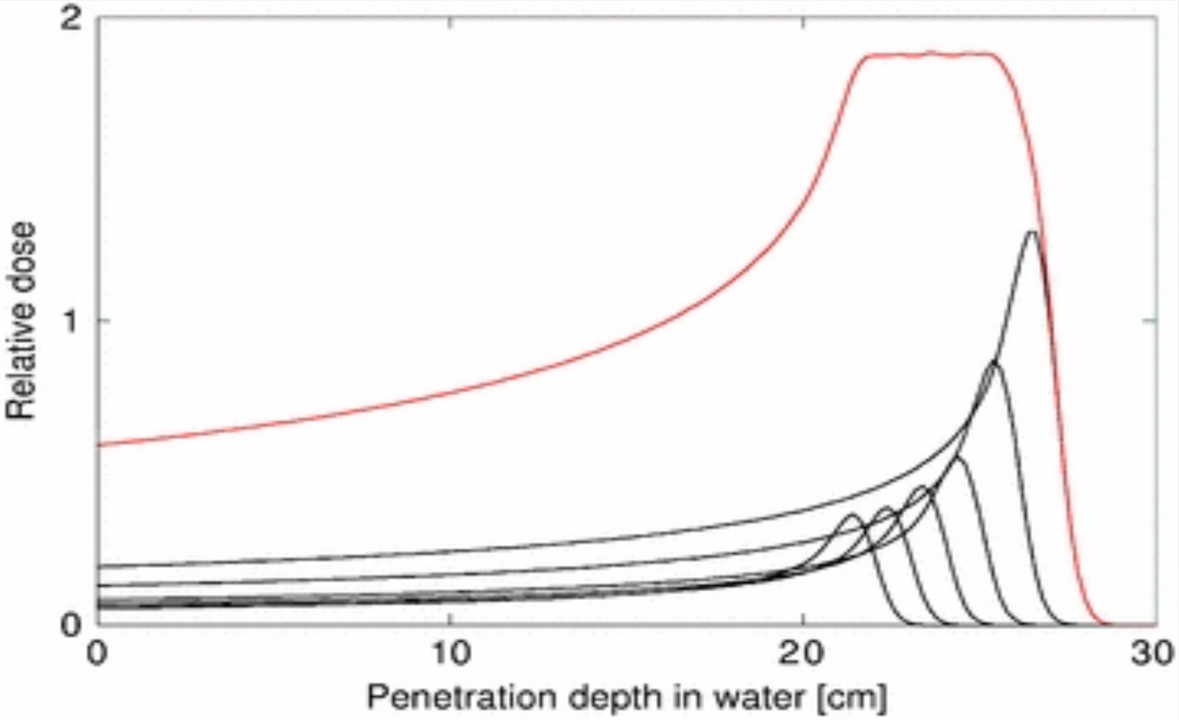
Spread out Breagg peak (SOBP)



Proton therapy
Alfred R Smith 2006 Phys. Med. Biol. 51 R491 doi:10.1088/0031-9155/51/13/R26

It is advantageous to widen the sharp Bragg peaks by passive systems or by overlapping beam with decreasing energies, in order to reduce the treatment time

Biological aspects

Biological effect

- **X-rays**

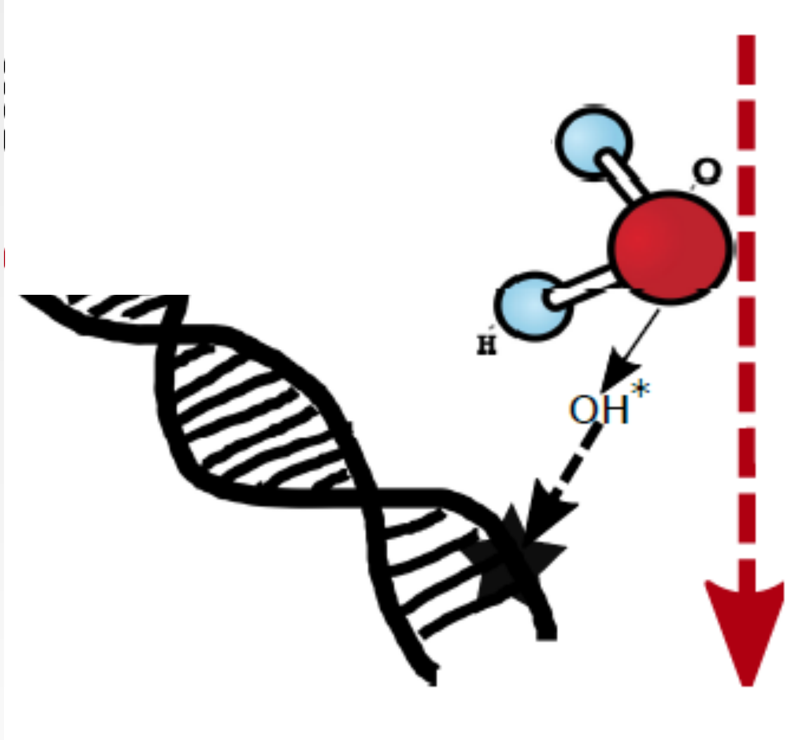
  X-rays produce a homogenous ionization producing large distances between neighboring damage sites

  Free radicals are responsible for DNA damage

  To make DNA damage permanent, the presence of oxygen is required to prevent the DNA repairing itself

  ➡Oxygen Enhancement Ratio (OER)

  Hypoxic condition makes tumor radio resistant



$$\mathrm{OER} = \frac{D_{hypoxic}}{D_{aerobic}}$$

Biological effect

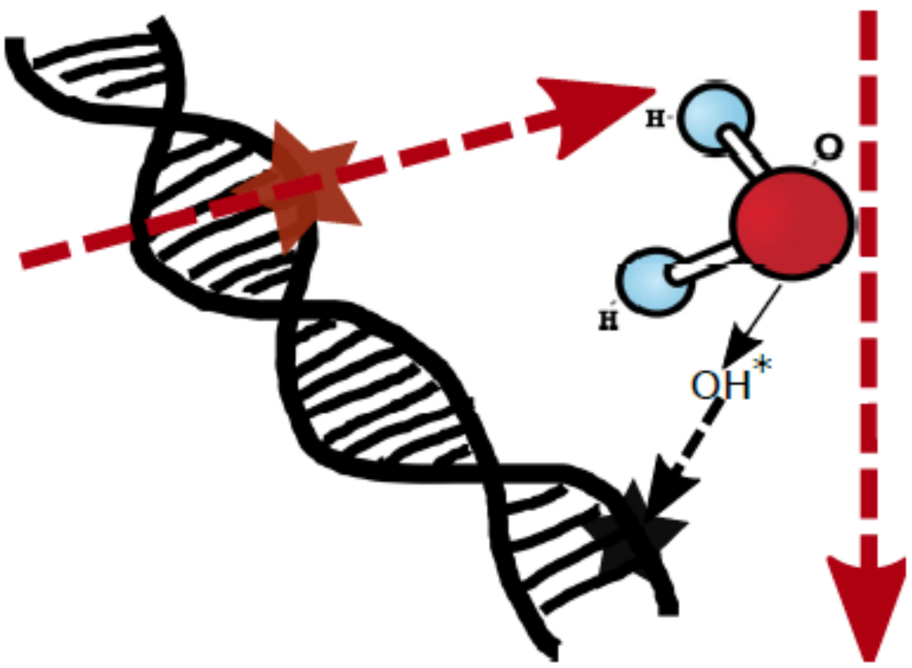
- **Ions**

  The typical extension of the track center with the highest “local” dose is on the order of nanometers

  large probability of correlated nearby DNA damages like single or double strand breaks or base damages.

  ➡Severe damages directly occur on the DNA

  The OER for ions is much lower than for photons

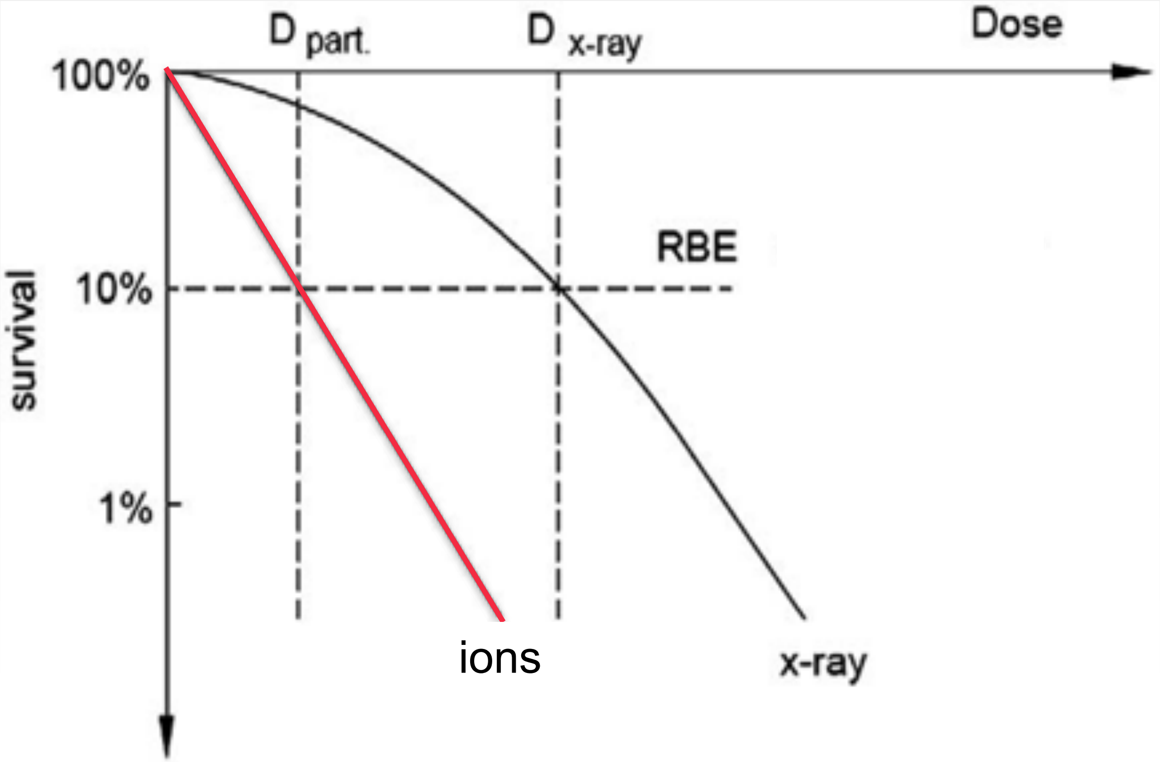


Biological effect

RBE : Relative biological effectiveness

$$\mathrm{RBE} = \frac{D_{ref}}{D_{ion}}$$

The ratio of the dose of a reference radiation (x-rays) to the dose of the radiation in question (e.g., ions) to produce an identical biological effect isoeffect (cell survival)



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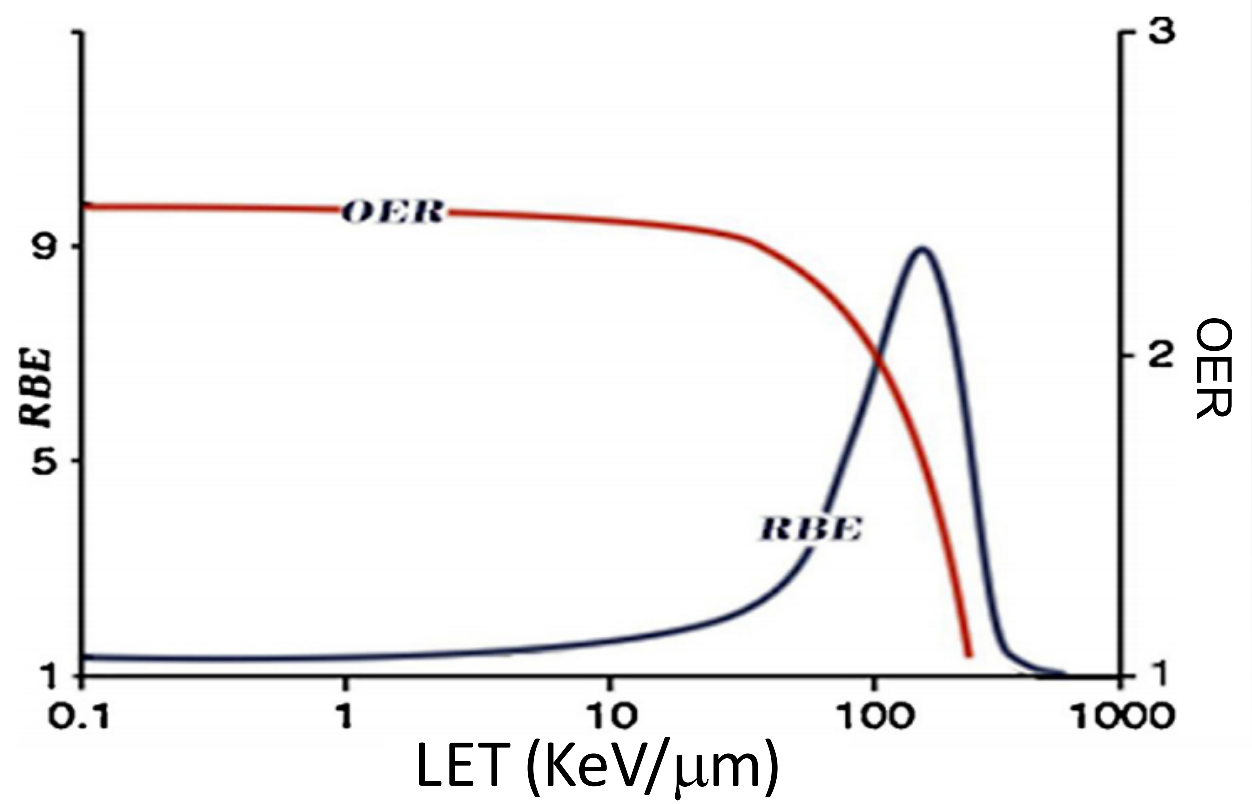
Biological effect

LET: Energy that is transferred by an ionizing particle to the medium along its path

For High-LET particles, in the Bragg peak area, the RBE increases notably while the OER is reduced almost to 1



Accelerators and gantries

Cyclotrons

➡ Easy to operate

➡ Highly reliable

➡ Compact machines

➡ Extremely stable and regulable beam intensities

- No energy variation
  The energy can be changed only by means of passive degraders in the beam line

Protons

Synchrotrons

➡ Fast energy variation from pulse to pulse

➡ Possibility to accelerate also heavy ions with high magnetic rigidity

- Injector needed
- Delicate extraction system
- More complex in operation

Heavy ions

Beam delivery systems

- ➡ Transport of particle beams to the treatment area
- ➡ Distribution of the beam over the planned target volume (**PTV**) accurately and homogeneously with the desired dose distribution

Fully passive systems

fixed beam modulation particle beam is adapted in three dimensions to the target volume only by passive non variable field shaping elements

Fully active beam scanning

the target volume is dissected in small volume elements voxels and a fine pencil beam is used to fill the voxels with the appropriate dose, ideally without any material in the beam path.

Many other solutions in between these two extremes are possible *(Chu et al. 1993)*

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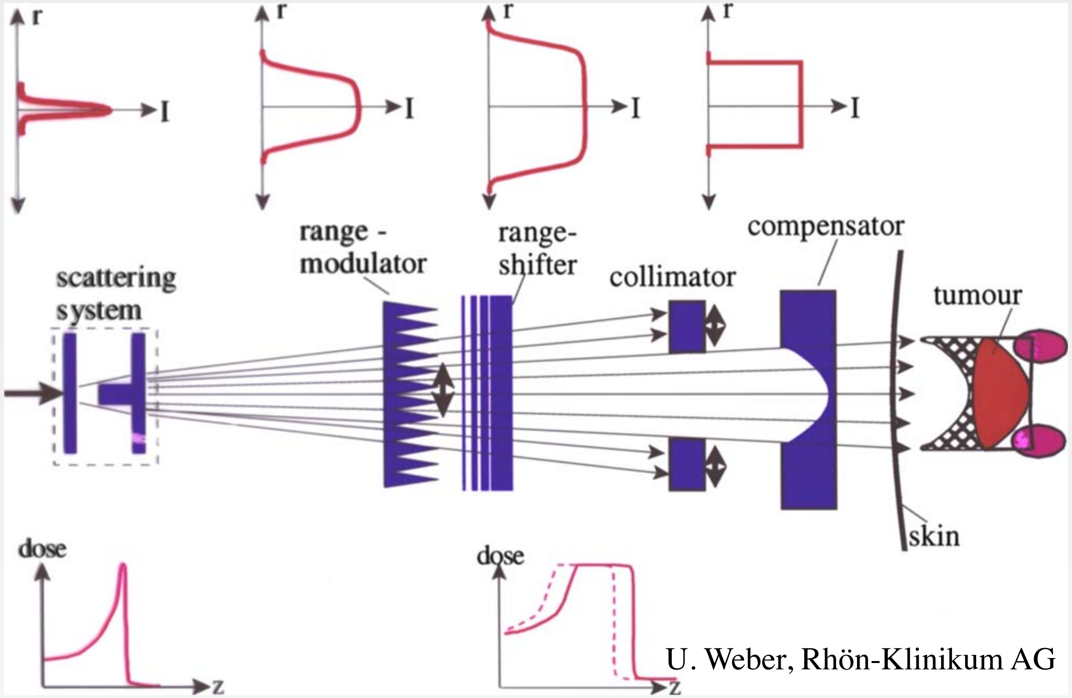
Fully passive system



U. Weber, Rhön-Klinikum AG

- ➡ Beam is broadened by a scattering system and adapted to the target volume by various passive beam shaping devices
- ➡ Adaption of the dose field to the distal contour of the target volume is achieved by a compensator
- Unwanted normal-tissue dose in the proximal part indicated by the doubly hatched area.

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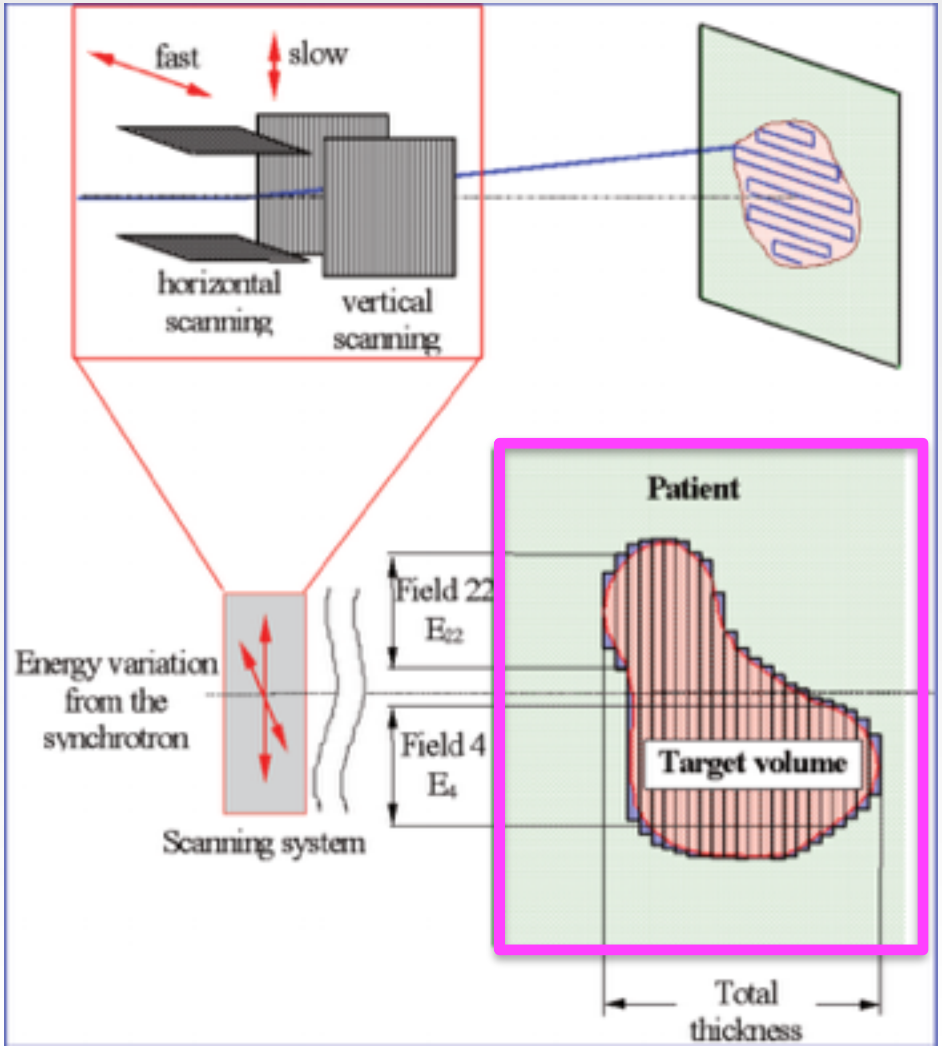
Fully active system



- Target volume sliced along its depth, each slice corresponds to a different penetration depth
- Irradiation of each slice by means of two orthogonal scanning magnets
- Energy changed by the synchrotron to irradiate each slice
- Possibility of intensity modulated proton therapy (IMPT)

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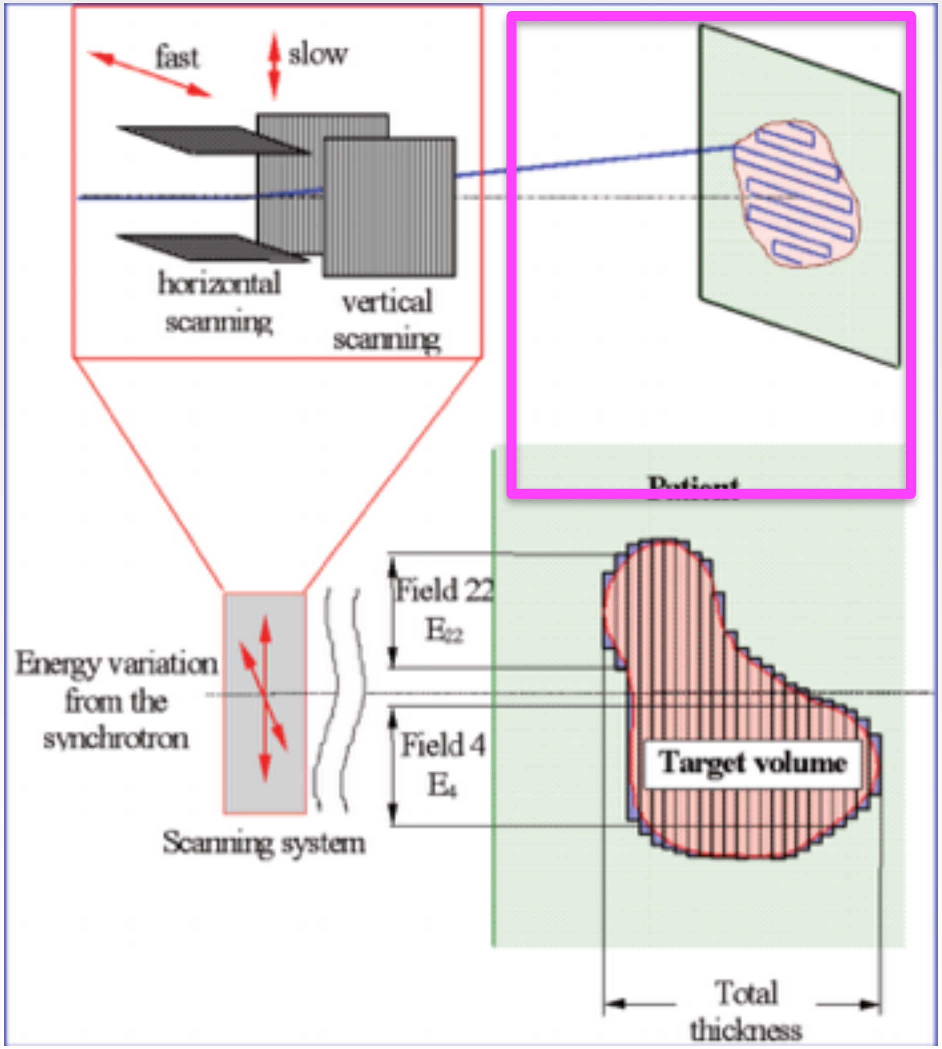
Fully active system



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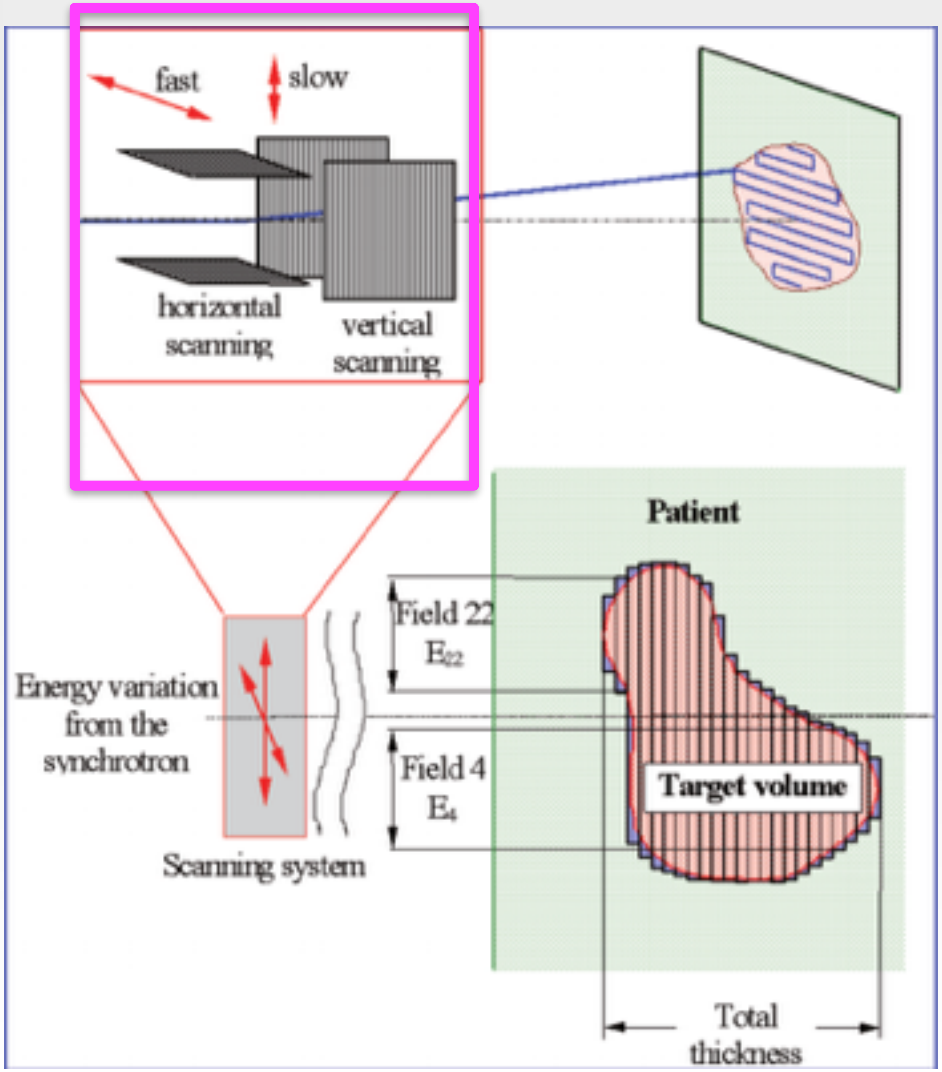

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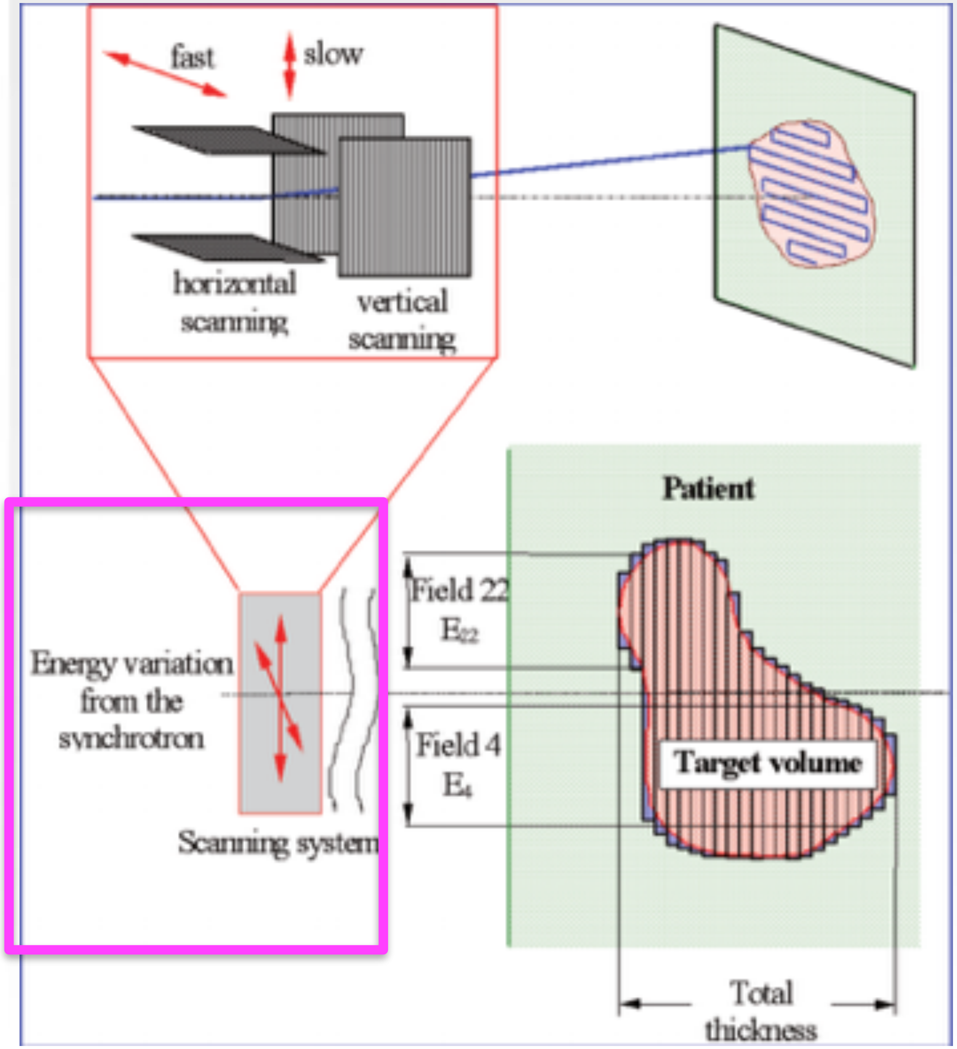

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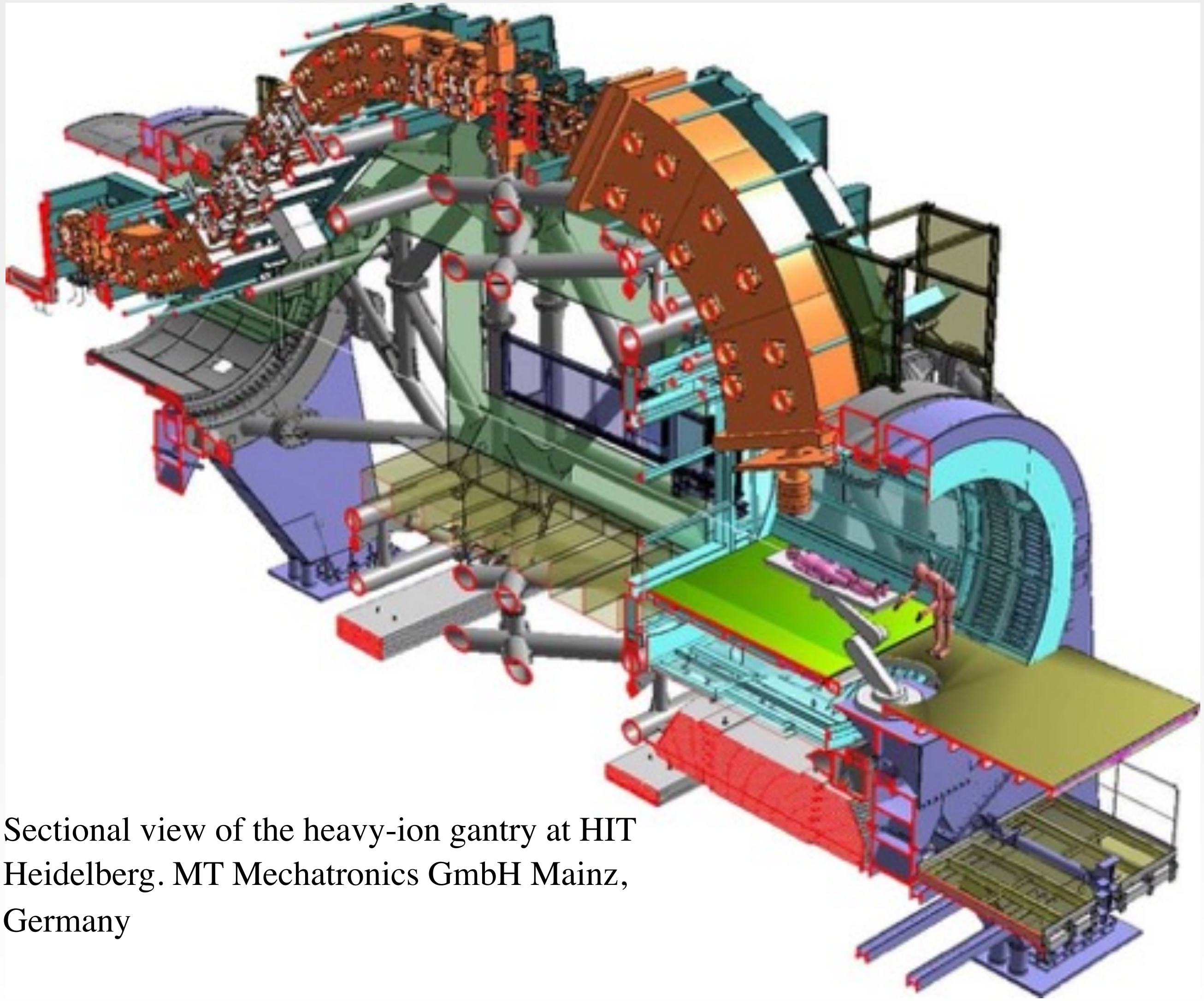
Gantries

- In conventional radiotherapy patients are treated in supine position, i.e., in the same position as used for imaging
- The electron linac is mounted on a rotational support structure, **gantry**, which in combination with the rotatable patient couch allows to select the beam directions and angles (0º-360°) for the patient treatment
- On non-medical accelerators the beam was delivered horizontally and patients were treated in either supine or sitting position
- The first gantry systems for protons started operation in 1990 at the Loma Linda University Medical Center USA, the first dedicated clinical proton therapy facility *(Slater et al., 1988)*

Gantries

- For heavy ions a high bending power is required and leads to correspondingly large dimensions for a gantry. The magnetic rigidity of 380 MeV/u carbon ions with a range of 25 cm in water is about three times higher than for 200 MeV protons with the same range.
- The first rotating isocentric gantry system for heavy ions was constructed at the HIT center Germany
- The rotating structure built by MT Mechatronics GmbH Mainz, Gemany is about 20 m long with a diameter of 13 m and a total weight of 670 tons

Gantries



Sectional view of the heavy-ion gantry at HIT Heidelberg. MT Mechatronics GmbH Mainz, Germany

Historical background

The advances in proton therapy are closely tied to advances in accelerator technology

Ernest O. Lawrence developed the cyclotron at the University of California Lawrence Berkeley Laboratory (LBL) in 1930 and won the Nobel Prize for this work in 1939

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184-inch Cyclotron: ~100MeV

1945

The first beam, 1947

The end, 1986

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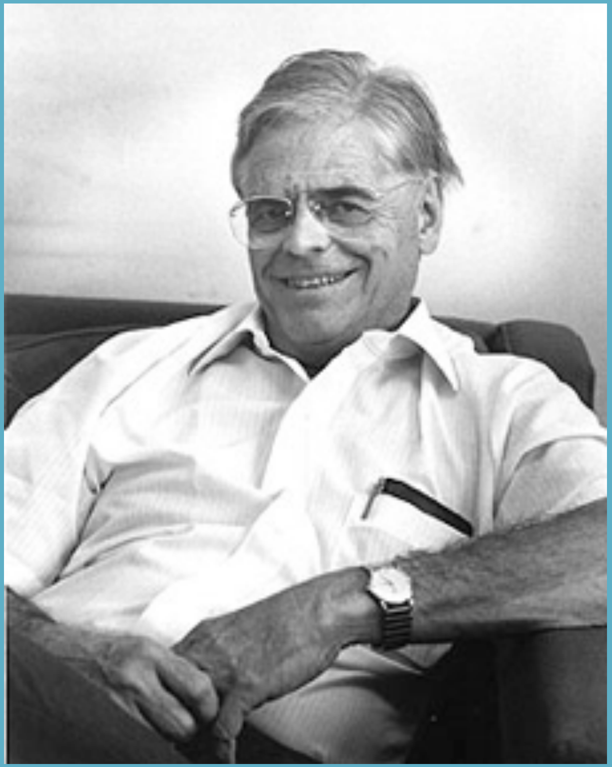
"These properties make it possible to irradiate intensely a <u>strictly localized region</u> within the body, with <u>but little skin dose</u>. It will be easy to produce well collimated narrow beams of fast protons, and since the range of the beam is easily controllable, <u>precision exposure of well defined small volumes within the body will soon be feasible.</u>"



Robert R. Wilson, 1946

Dose Localization
Lower entrance dose
No or low exit dose

The Beginning of Particle Beam Therapy: Berkeley (LBL)

- **1948**: Biology experiments using protons
- **1952**: Human exposure to accelerated proton, deuteron and helium ion beams
- Pituitary gland treated with beams passing entirely through the brain in a path that intersected the pituitary gland *(Tobias et al. 1958)*
- **1956-1986**: Clinical Trials– 1500 patients treated with p and ^{4}He

Prof. Cornelius A. Tobias

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The Svedberg Laboratory in Uppsala (former Gustaf Werner Institute)

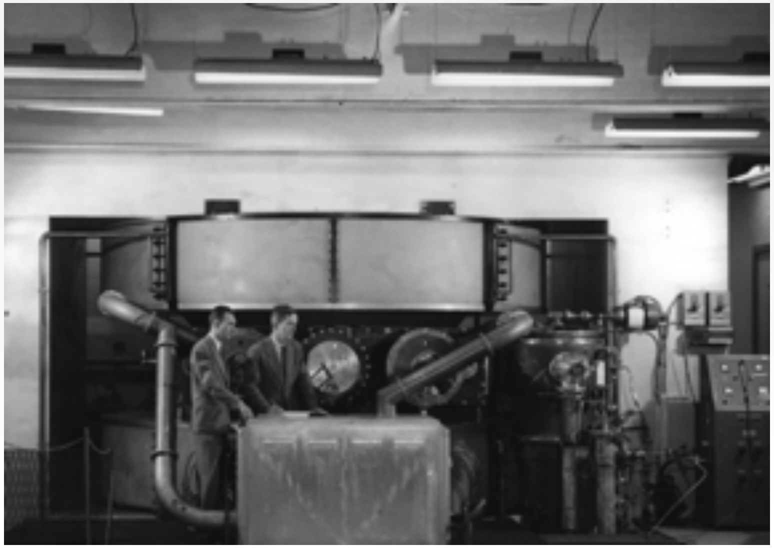
- **1949:** Built the synchrocyclotron at the Gustav Werner Institute (Uppsala)
- **1950s:** Pre-therapeutic physical experiments with high energy protons (*Larsson et al. 1958*)
- **1957:** First patient treated with proton beam
- **1994:** The cyclotron was upgraded at Theodor Svedberg Laboratory

Prof. Börje Larsson (1931-1998)

Börje Larsson and Theodor Svedberg

Harvard Cyclotron Laboratory, Cambridge (HCL)

- **1938:** First Harvard Cyclotron completed (Bainbridge, Street and Hickman)
- **1943:** Moved the cyclotron to Los Alamos (RR Wilson)
- **1949:** Second Harvard Cyclotron completed (Norman F. Ramsey): 95-110 MeV protons
- **1955:** Second Harvard Cyclotron: 165 MeV protons
- **1962:** Proton radiotherapy - first steps (*Kelleberg et al. 1962*)
- **1972:** Clinical trials with protons (Suit, Koehler, Goitein, Richard Wilson)



Around the world

Russia

- **1968**: Joint Institute for Nuclear Research in Dubna
- **1969**: the Moscow Institute for Theoretical and Experimental Physics in 1969
- **1975**: St Petersburg in 1975.

Japan

- **1979**: first treatments at the National Institute for Radiological Sciences in Chiba, Japan
- **1980**: development of a spot scanning system for proton treatment delivery

More

- **1989**: Clatterbridge, England
- **1991**: Nice and Orsay, France
- **1993**: iThemba Labs in Cape Town, South Africa
- **1996**: PSI at Villigen, Switzerland
- **1998**: HMI in Berlin, Germany
- **1998** NCC in Kashiwa, Japan
- **1999**: Dubna, Russia (1999)

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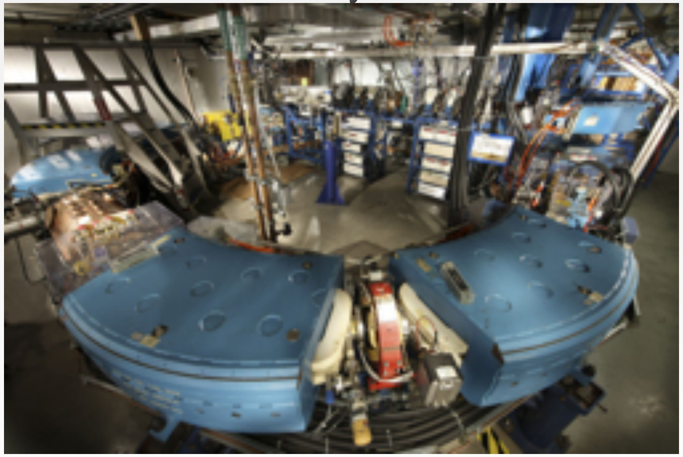
BEVALAC accelerator, LBL Berkeley

- **1971**: Heavy ions accelerated at BEVALAC synchrotron
- **1975**: Physicians and medical physicists from the University of California at San Francisco provided the medical expertise for the first **heavy ion** treatments *(Lyman et al. 1979)*
- **1992:** End of the hadrontherapy project

Harry Heckman, Ed McMillan, Cornelius Tobias, Tom Budinger, Ed Lofgren, Walt Hartsough (l. to r.)

First medical accelerator, Loma Linda, CA

- **1990**: first patient treatments at the Loma Linda University Medical Center (LLUMC) *(Slater et al 1991)*
- The facility was the result of the vision and work of Dr James Slater who was the Chairman of the Department of Radiation Medicine.
- 250 MeV synchrotron and three isocentric gantries designed and built at Fermi National Laboratory.
- A very efficient proton treatment planning program was developed, enabling the LLUMC group to treat the largest number of patients (about 10500) of any proton treatment facility (*Miller 1995, Chu et al 1993*)



Proton beam accelerator at Loma Linda University Medical Center

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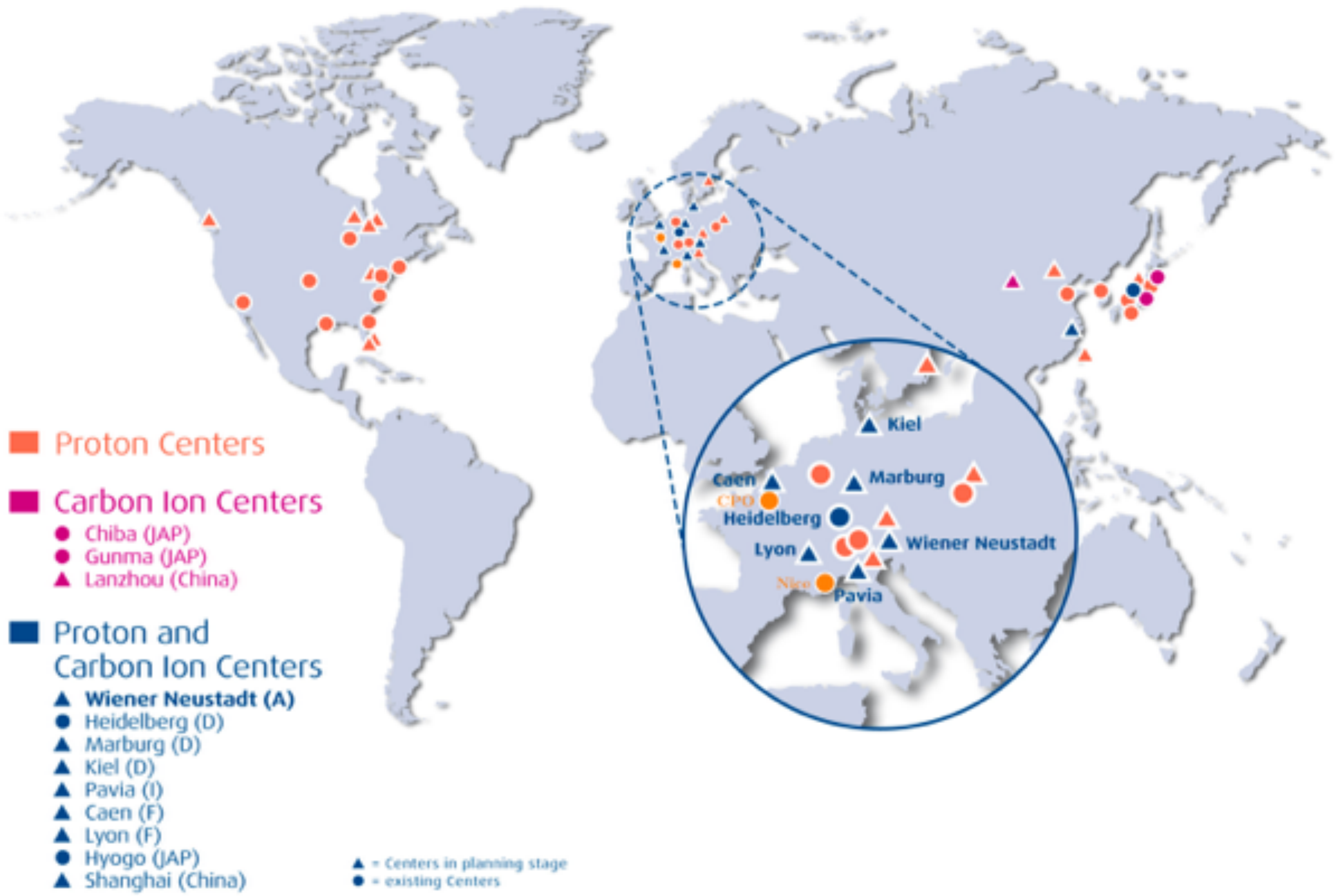
Hadron therapy centers in 2011



Hadron therapy centers in September 2019

COUNTRY	WHO, WHERE	PARTICLE	S/C/SC*	BEAM DIRECTIONS	START
Italy	CNAO, Pavia	C-ion	S 480/u	3 horiz., 1 vertical, fixed beams	2012
USA, NJ.	ProCure Proton Therapy Center, Somerset	p	C 230	4 gantries***	2012
Germany	WPE, Essen	p	C 230	4 gantries***, 1 fixed beam	2013
Japan	Nagoya PTC, Nagoya City, Aichi	p	S 250	2 gantries***, 1 fixed beam	2013
Japan	SAGA-HIMAT, Tosu	C-ion	S 400/u	3 horiz., vertical, 45 deg., fixed beams	2013
USA, WA.	SCCA ProCure Proton Therapy Center, Seattle	p	C 230	4 gantries***	2013
USA, MO.	S. Lee Kling PTC, Barnes Jewish Hospital, St. Louis	p	SC 250	1 gantry	2013
China	SPHIC, Shanghai	p	S 250	3 fixed beams**	2014
China	SPHIC, Shanghai	C-ion	S 430/u	3 fixed beams**	2014
Germany	UPTD, Dresden	p	C 230	1 gantry***	2014
Italy	APSS, Trento	p	C 230	2 gantries**, 1 fixed beams	2014
Japan	Hokkaido Univ. Hospital PBTC, Hokkaido	p	S 220	1 gantry	2014
Japan	Aizawa Hospital PTC, Nagano	p	C 235	1 gantry	2014
USA, TN.	ProVision Cancer Cares Proton Therapy Center, Knoxville	p	C 230	3 gantries**	2014
USA, CA.	California Protons Cancer Therapy Center, San Diego	p	C 250	3 gantries**, 2 horiz. fixed beams**	2014
USA, LA.	Willis Knighton Proton Therapy Cancer Center, Shreveport	p	C 230	1 gantry**	2014
Germany	MIT, Marburg	p	S 250	3 horiz., 1 45deg. fixed beams**	2015
Germany	MIT, Marburg	C-ion	S 430/u	3 horiz., 1 45deg. fixed beams**	2015
Japan	i-Rock Kanagawa Cancer Center, Yokohama	C-ion	S 430/u	4 horiz., 2 vertical, fixed beams	2015
South Korea	Samsung PTC, Seoul	p	C 230	2 gantries	2015
Sweden	The Skandion Clinic,Uppsala	p	C 230	2 gantries**	2015
Taiwan	Chang Gung Memorial Hospital, Taipei	p	C 230	4 gantries**, 1 fixed beam exp.	2015
USA, FL.	Ackerman Cancer Center, Jacksonville	p	SC 250	1 gantry	2015
USA, MN.	Mayo Clinic Proton Beam Therapy Center, Rochester	p	S 220	4 gantries**	2015
USA, NJ.	Wood Johnson Univ. Hospital, New Brunswick	p	SC 250	1 gantry	2015
USA, TX.	Texas Center for Proton Therapy, Irving	p	C 230	2 gantries**, 1 horiz. fixed beam	2015
USA, TN.	St. Jude Red Frog Events Proton Therapy Center, Memphis	p	S 220	2 gantries**, 1 horiz. fixed beam	2015
Austria	MedAustron, Wiener Neustadt	p	S 253	2 horiz., 1 vertical fixed beam**,	2016
Japan	Tsuyama Chuo Hospital, Okayama	p	S 235	1 gantry	2016
Russia	MRRC, Obninsk	p	S 250	1 fixed beam	2016
USA, AZ.	Mayo Clinic Proton Therapy Center, Phoenix	p	S 220	4 gantries**	2016
USA, MD.	Maryland Proton Treatment Center, Baltimore	p	C 250	4 gantries**, 1 horiz. fixed beam**	2016
USA, FL.	Orlando Health PTC, Orlando	p	SC 250	1 gantry	2016
USA, OH.	UH Sideman CC, Cleveland	p	SC 250	1 gantry	2016
USA, OH.	Cincinnati Children's Proton Therapy Center, Cincinnati	p	C 250	3 gantries**	2016
Japan	Hakuhokai Group Osaka PT Clinic, Osaka	p	S 235	1 gantry	2017
Japan	Kobe Proton Center, Kobe	p	S 235	1 gantry	2017
USA, MI.	Beaumont Health Proton Therapy Center, Detroit	p	C 230	1 gantry**	2017
USA, FL.	Baptist Hospital's Cancer Institute PTC, Miami	p	C 230	3 gantries**	2017
England	Proton Partner's Rutherford CC, Newport	p	C 230	1 gantry**	2018
England	The Christie Proton Therapy Center, Manchester	p	C 250	3 gantries**	2018
France	CYCLHAD, Caen	p	C 230	1 gantry**	2018
Japan	Narita Memorial Proton Center, Toyohgashi	p	C 230	1 gantry**	2018
Japan	Osaka Heavy Ion Therapy Center, Osaka	C-ion	S 430/u	3 fixed beams, 6 ports**	2018
Russia	MIBS, Saint-Petersburg	p	C 250	2 gantries**	2018
The Netherlands	UMC PTC, Groningen	p	C 230	2 gantries***	2018
The Netherlands	HollandPTC, Delft	p	C 250	2 gantries**, 1 horiz. fixed beam**	2018
USA, DC.	MedStar Georgetown University Hospital PTC, Washington	p	SC 250	1 gantry**	2018
USA, TN.	Provision CARES Proton Therrapy Center, Nashville	p	C 230	2 gantries**	2018
USA, GA.	Emory Proton Therapy Center, Atlanta	p	C 250	3 gantries**, 2 horiz. fixed beams**	2018
Austria	MedAustron, Wiener Neustadt	C-ion	S 403/u	2 horiz. and 1 verticalfixed beam**	2019
China	Heavy Ion Cancer Treatment Center, Wuwei, Gansu	C-ion	S 400/u	4 fixed beams**	2019
Denmark	Dansk Center for Partikelterapi, Aarhus	p	C 250	3 gantries**, 1 horiz. fixed beam**	2019
India	Apollo Hospitals PTC, Chennai	p	C 230	2 gantries, 1 fixed beam**	2019
The Netherlands	ZON PTC, Maastricht	p	SC 250	1 gantry**	2019
USA, OK.	Stephensen Cancer Center, Oklahoma	p	SC 250	1 gantry**	2019
USA, MI.	McLaren PTC, Flint	p	S 250/330	3 gantries**	2019
USA, NY.	The New York Proton Center, East Harlem, New York	p	C 250	3 gantries**	2019

https://www.ptcog.ch/index.php/facilities-in-operation

Hadron therapy centers under construction

Particle therapy facilities under construction (update September 2019)

COUNTRY	WHO, WHERE	PARTICLE(S)	MAX. ENERGY (MeV) ACCELERATOR TYPE (VENDOR)*	BEAM DIRECTIONS	NO. OF TREATMENT ROOMS	START OF TREATMENT PLANNED
Belgium	ParTICLe, Leuven	p	230 SC cyclotron (IBA)	1 gantry (PBS), 1 horiz. beamline (research)	2	2019
China	HITFil at IMP, Lanzhou, Gansu	C-ion	400/u synchrotron (?)	4 horiz., vertical, oblique, fixed beams	4	2019
China	Ruijin Hospital, Jiao Tong University, Shanghai	p	250 synchrotron (Apactron)	1 gantry, 2 horiz. fixed beams	3	2020
China	Zhuozhou Proton Therapy Center, Baoding, Hebei	p	230 cyclotron (IBA)	4 gantries, 1 horiz. fixed beam	5	2019
China	Guangdong Hengjian Medical Technologies Co., Guangzhou	p	230 cyclotron (IBA)	3 gantries	3	2020
China	Qingdao Zhong Jia Lian He Healthcare, Shandong	p	230 cyclotron (IBA)	4 gantries, 1 fixed beam	5	2019
China	Beijing Proton Center, Beijing	p	230 cyclotron (?)	3 gantries, 1 horiz. fixed beam	4	2020?
China	HIMC Center, Hefei, Anhui	p	250 SC cyclotron (Varian)	3 gantries, 1 horiz. fixed beam	4	2020?
China	Guangzhou Concord Cancer Center, GCCC, Guangdong	p	250 SC cyclotron (Varian)	4 gantries	4	2021
Emirate of Abu Dhabi	Proton Partners Int., Abu Dhabi	p	230 cyclotron (IBA)	1 gantry, 1 horiz. fixed beam	1	2019
France	ARCHADE, Caen	C-ion	400/u cyclotron (IBA)	1 fixed beam (r&d)	1	2023
India	Tata Memorial Centre, Mumbai	p	230 cyclotron (IBA)	3 gantries	3	2019
India	Health Care Global	p	250 SC cyclotron (Varian)	1 gantry	1	2020
Japan	Social Medical Corporation Kouseikai Takai Hospital, Tenri City, Nara Pref.	p	230 cyclotron (Sumitomo)	1 gantry	1	2018

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Hadron therapy centers under construction

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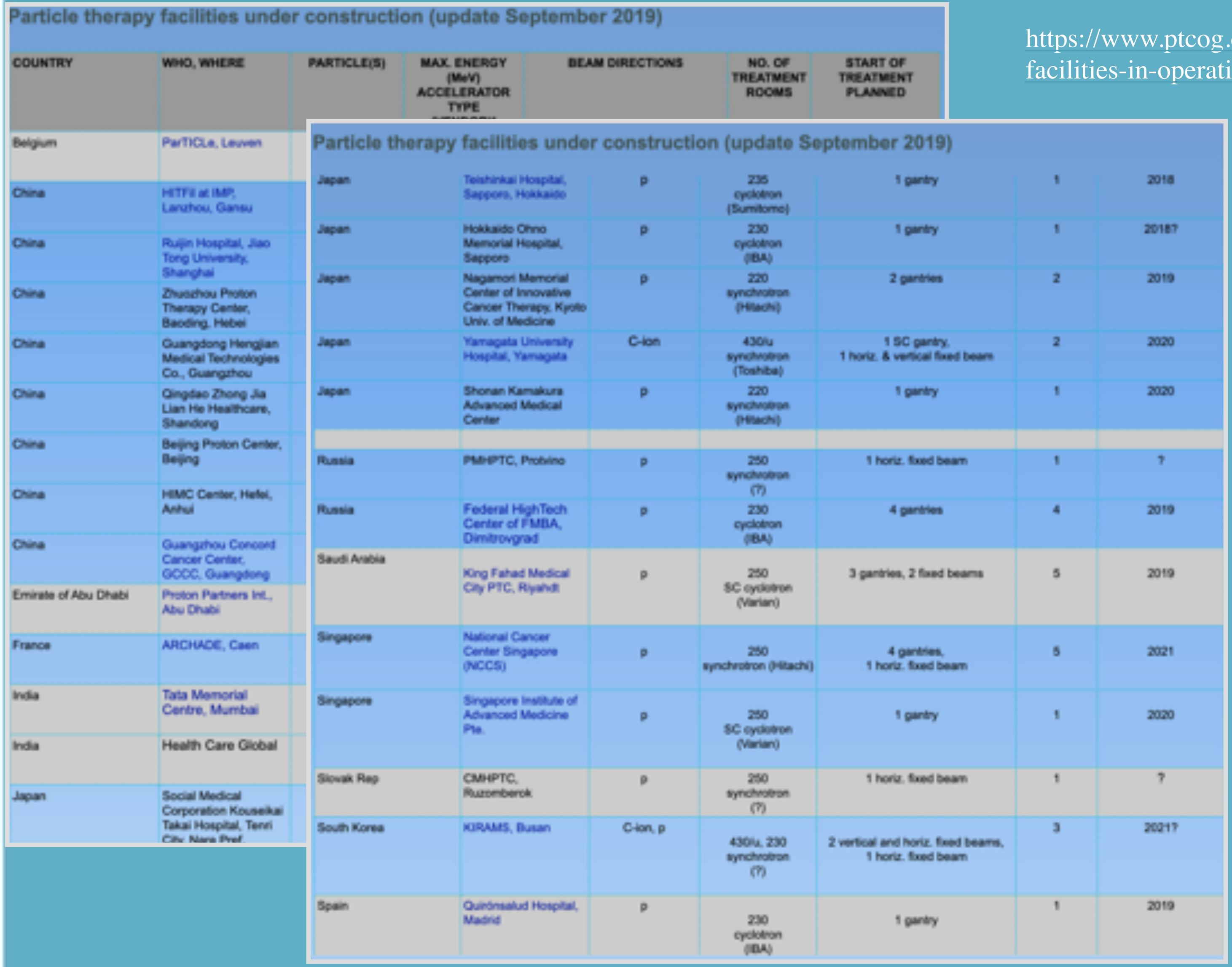

Particle therapy facilities under construction (update September 2019)

COUNTRY	WHO, WHERE	PARTICLE(S)	MAX. ENERGY (MeV) ACCELERATOR TYPE	BEAM DIRECTIONS	NO. OF TREATMENT ROOMS	START OF TREATMENT PLANNED
Belgium	ParTICLe, Leuven					
China	HITFil at IMP, Lanzhou, Gansu					
China	Ruijin Hospital, Jiao Tong University, Shanghai					
China	Zhuozhou Proton Therapy Center, Baoding, Hebei					
China	Guangdong Hengjian Medical Technologies Co., Guangzhou					
China	Qingdao Zhong Jia Lian He Healthcare, Shandong					
China	Beijing Proton Center, Beijing					
China	HIMC Center, Hefei, Anhui					
China	Guangzhou Concord Cancer Center, GCCC, Guangdong					
Emirate of Abu Dhabi	Proton Partners Int., Abu Dhabi					
France	ARCHADE, Caen					
India	Tata Memorial Centre, Mumbai					
India	Health Care Global					
Japan	Social Medical Corporation Kouseikai Takai Hospital, Tenri City, Nara Pref.					

Particle therapy facilities under construction (update September 2019)

Japan	Teishinkai Hospital, Sapporo, Hokkaido	p	235 cyclotron (Sumitomo)	1 gantry	1	2018
Japan	Hokkaido Ohno Memorial Hospital, Sapporo	p	230 cyclotron (IBA)	1 gantry	1	2018?
Japan	Nagamori Memorial Center of Innovative Cancer Therapy, Kyoto Univ. of Medicine	p	220 synchrotron (Hitachi)	2 gantries	2	2019
Japan	Yamagata University Hospital, Yamagata	C-ion	430/u synchrotron (Toshiba)	1 SC gantry, 1 horiz. & vertical fixed beam	2	2020
Japan	Shonan Kamakura Advanced Medical Center	p	220 synchrotron (Hitachi)	1 gantry	1	2020
Russia	PMHPTC, Protvino	p	250 synchrotron (?)	1 horiz. fixed beam	1	?
Russia	Federal HighTech Center of FMBA, Dimitrovgrad	p	230 cyclotron (IBA)	4 gantries	4	2019
Saudi Arabia	King Fahad Medical City PTC, Riyahdt	p	250 SC cyclotron (Varian)	3 gantries, 2 fixed beams	5	2019
Singapore	National Cancer Center Singapore (NCCS)	p	250 synchrotron (Hitachi)	4 gantries, 1 horiz. fixed beam	5	2021
Singapore	Singapore Institute of Advanced Medicine Pte.	p	250 SC cyclotron (Varian)	1 gantry	1	2020
Slovak Rep	CMHPTC, Ruzomberok	p	250 synchrotron (?)	1 horiz. fixed beam	1	?
South Korea	KIRAMS, Busan	C-ion, p	430/u, 230 synchrotron (?)	2 vertical and horiz. fixed beams, 1 horiz. fixed beam	3	2021?
Spain	Quirónsalud Hospital, Madrid	p	230 cyclotron (IBA)	1 gantry	1	2019

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Hadron therapy centers under construction

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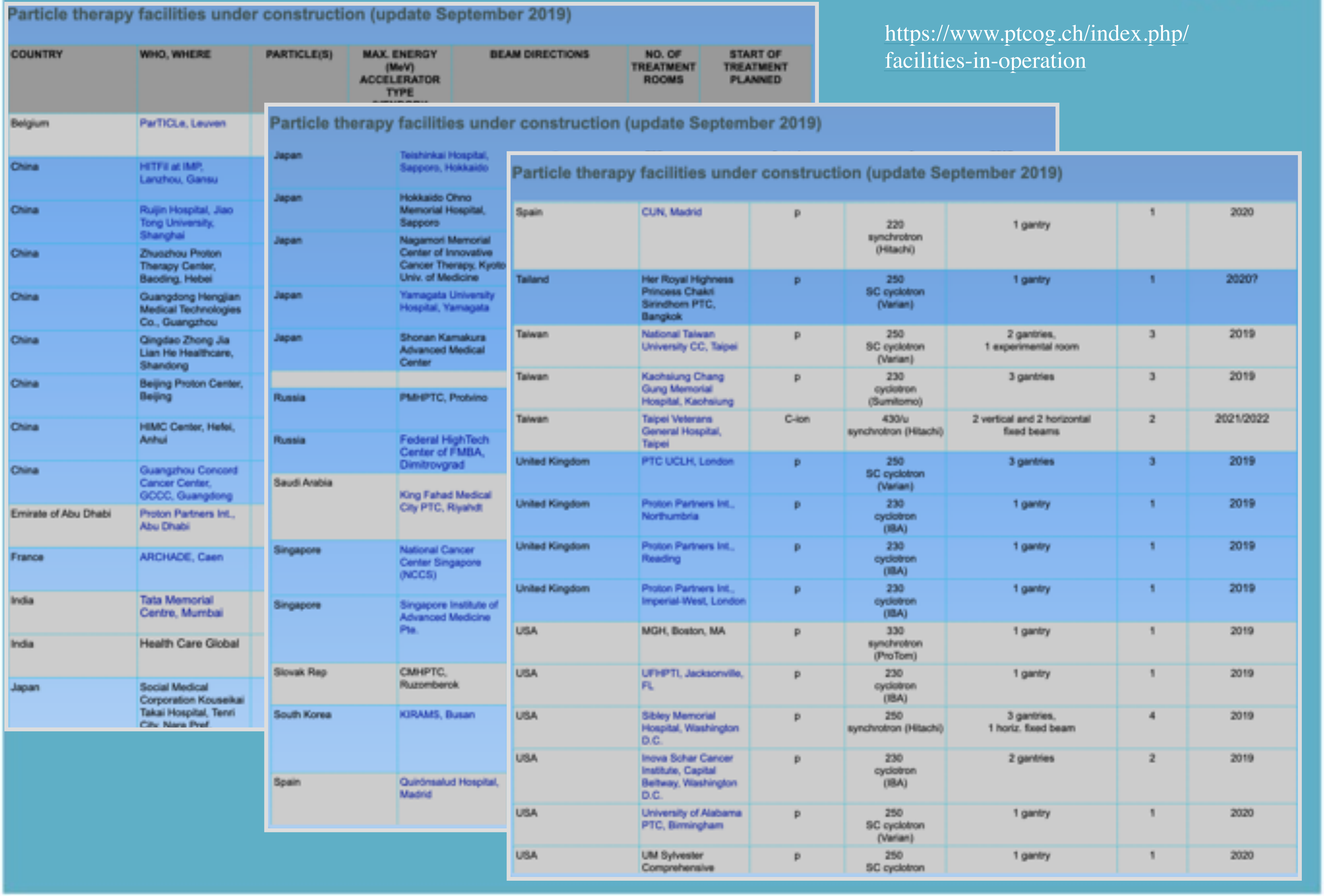


Particle therapy facilities under construction (update September 2019)

COUNTRY	WHO, WHERE	PARTICLE(S)	MAX. ENERGY (MeV) ACCELERATOR TYPE	BEAM DIRECTIONS	NO. OF TREATMENT ROOMS	START OF TREATMENT PLANNED
Belgium	ParTICLe, Leuven					
China	HITFil at IMP, Lanzhou, Gansu					
China	Ruijin Hospital, Jiao Tong University, Shanghai					
China	Zhuozhou Proton Therapy Center, Baoding, Hebei					
China	Guangdong Hengjian Medical Technologies Co., Guangzhou					
China	Qingdao Zhong Jia Lian He Healthcare, Shandong					
China	Beijing Proton Center, Beijing					
China	HIMC Center, Hefei, Anhui					
China	Guangzhou Concord Cancer Center, GCCC, Guangdong					
Emirate of Abu Dhabi	Proton Partners Int., Abu Dhabi					
France	ARCHADE, Caen					
India	Tata Memorial Centre, Mumbai					
India	Health Care Global					
Japan	Social Medical Corporation Kouseikai Takai Hospital, Tenri City, Nara Pref.					

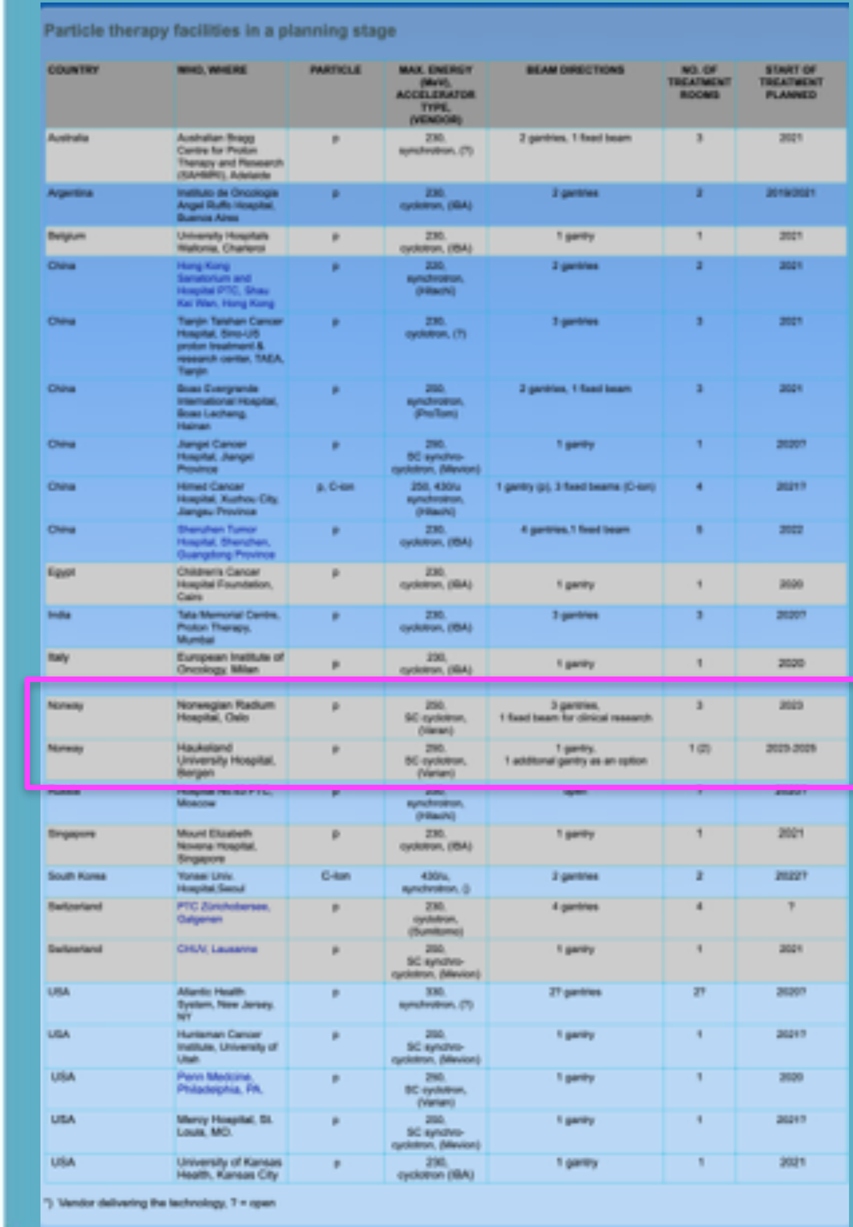
Particle therapy facilities under construction (update September 2019)

Japan	Teishinkai Hospital, Sapporo, Hokkaido
Japan	Hokkaido Ohno Memorial Hospital, Sapporo
Japan	Nagamori Memorial Center of Innovative Cancer Therapy, Kyoto Univ. of Medicine
Japan	Yamagata University Hospital, Yamagata
Japan	Shonan Kamakura Advanced Medical Center
Russia	PMHPTC, Protvino
Russia	Federal HighTech Center of FMBA, Dimitrovgrad
Saudi Arabia	King Fahad Medical City PTC, Riyahdt
Singapore	National Cancer Center Singapore (NCCS)
Singapore	Singapore Institute of Advanced Medicine Pte.
Slovak Rep	CMHPTC, Ruzomberok
South Korea	KIRAMS, Busan
Spain	Quirónsalud Hospital, Madrid

Particle therapy facilities under construction (update September 2019)

Spain	CUN, Madrid	p	220 synchrotron (Hitachi)	1 gantry	1	2020
Tailand	Her Royal Highness Princess Chakri Sirindhorn PTC, Bangkok	p	250 SC cyclotron (Varian)	1 gantry	1	2020?
Taiwan	National Taiwan University CC, Taipei	p	250 SC cyclotron (Varian)	2 gantries, 1 experimental room	3	2019
Taiwan	Kaohsiung Chang Gung Memorial Hospital, Kaohsiung	p	230 cyclotron (Sumitomo)	3 gantries	3	2019
Taiwan	Taipei Veterans General Hospital, Taipei	C-ion	430/u synchrotron (Hitachi)	2 vertical and 2 horizontal fixed beams	2	2021/2022
United Kingdom	PTC UCLH, London	p	250 SC cyclotron (Varian)	3 gantries	3	2019
United Kingdom	Proton Partners Int., Northumbria	p	230 cyclotron (IBA)	1 gantry	1	2019
United Kingdom	Proton Partners Int., Reading	p	230 cyclotron (IBA)	1 gantry	1	2019
United Kingdom	Proton Partners Int., Imperial-West, London	p	230 cyclotron (IBA)	1 gantry	1	2019
USA	MGH, Boston, MA	p	330 synchrotron (ProTom)	1 gantry	1	2019
USA	UFHPTI, Jacksonville, FL	p	230 cyclotron (IBA)	1 gantry	1	2019
USA	Sibley Memorial Hospital, Washington D.C.	p	250 synchrotron (Hitachi)	3 gantries, 1 horiz. fixed beam	4	2019
USA	Inova Schar Cancer Institute, Capital Beltway, Washington D.C.	p	230 cyclotron (IBA)	2 gantries	2	2019
USA	University of Alabama PTC, Birmingham	p	250 SC cyclotron (Varian)	1 gantry	1	2020
USA	UM Sylvester Comprehensive	p	250 SC cyclotron	1 gantry	1	2020

Hadron therapy centers in planning stage



Particle therapy facilities in a planning stage

COUNTRY	WHO, WHERE	PARTICLE	MAX. ENERGY (MeV), ACCELERATOR TYPE, (VENDOR*)	BEAM DIRECTIONS	NO. OF TREATMENT ROOMS	START OF TREATMENT PLANNED
Australia	Australian Bragg Centre for Proton Therapy and Research (SAHMRI), Adelaide	p	330, synchrotron, (?)	2 gantries, 1 fixed beam	3	2021
Argentina	Instituto de Oncologia Angel Roffo Hospital, Buenos Aires	p	230, cyclotron, (IBA)	2 gantries	2	2019/2021
Belgium	University Hospitals Wallonia, Charleroi	p	230, cyclotron, (IBA)	1 gantry	1	2021
China	Hong Kong Sanatorium and Hospital PTC, Shau Kei Wan, Hong Kong	p	230, synchrotron, (Hitachi)	2 gantries	2	2021
China	Tianjin Taishan Cancer Hospital, Sino-US proton treatment & research center, TAEA, Tianjin	p	230, cyclotron, (?)	3 gantries	3	2021
China	Boao Evergrande International Hospital, Boao Lecheng, Hainan	p	250, synchrotron, (ProTom)	2 gantries, 1 fixed beam	3	2021
China	Jiangxi Cancer Hospital, Jiangxi Province	p	250, SC synchro-cyclotron, (Mevion)	1 gantry	1	2020?
China	Himed Cancer Hospital, Xuzhou City, Jiangsu Province	p, C-ion	250, 430/u synchrotron, (Hitachi)	1 gantry (p), 3 fixed beams (C-ion)	4	2021?
China	Shenzhen Tumor Hospital, Shenzhen, Guangdong Province	p	230, cyclotron, (IBA)	4 gantries,1 fixed beam	5	2022
Egypt	Children's Cancer Hospital Foundation, Cairo	p	230, cyclotron, (IBA)	1 gantry	1	2020
India	Tata Memorial Centre, Proton Therapy, Mumbai	p	230, cyclotron, (IBA)	3 gantries	3	2020?
Italy	European Institute of Oncology, Milan	p	230, cyclotron, (IBA)	1 gantry	1	2020
Norway	Norwegian Radium Hospital, Oslo	p	250, SC cyclotron, (Varian)	3 gantries, 1 fixed beam for clinical research	3	2023
Norway	Haukeland University Hospital, Bergen	p	250, SC cyclotron, (Varian)	1 gantry, 1 additional gantry as an option	1 (2)	2023-2025
[illegible]	[illegible] PTC, Moscow	p	[illegible] synchrotron, (Hitachi)	open	[illegible]	[illegible]
Singapore	Mount Elizabeth Novena Hospital, Singapore	p	230, cyclotron, (IBA)	1 gantry	1	2021
South Korea	Yonsei Univ. Hospital,Seoul	C-ion	430/u, synchrotron, ()	2 gantries	2	2022?
Switzerland	PTC Zürichobersee, Galgenen	p	230, cyclotron, (Sumitomo)	4 gantries	4	?
Switzerland	CHUV, Lausanne	p	250, SC synchro-cyclotron, (Mevion)	1 gantry	1	2021
USA	Atlantic Health System, New Jersey, NY	p	330, synchrotron, (?)	2? gantries	2?	2020?
USA	Huntsman Cancer Institute, University of Utah	p	250, SC synchro-cyclotron, (Mevion)	1 gantry	1	2021?
USA	Penn Medicine, Philadelphia, PA	p	250, SC cyclotron, (Varian)	1 gantry	1	2020
USA	Mercy Hospital, St. Louis, MO	p	250, SC synchro-cyclotron, (Mevion)	1 gantry	1	2021?
USA	University of Kansas Health, Kansas City	p	230, cyclotron (IBA)	1 gantry	1	2021

*) Vendor delivering the technology, ? = open

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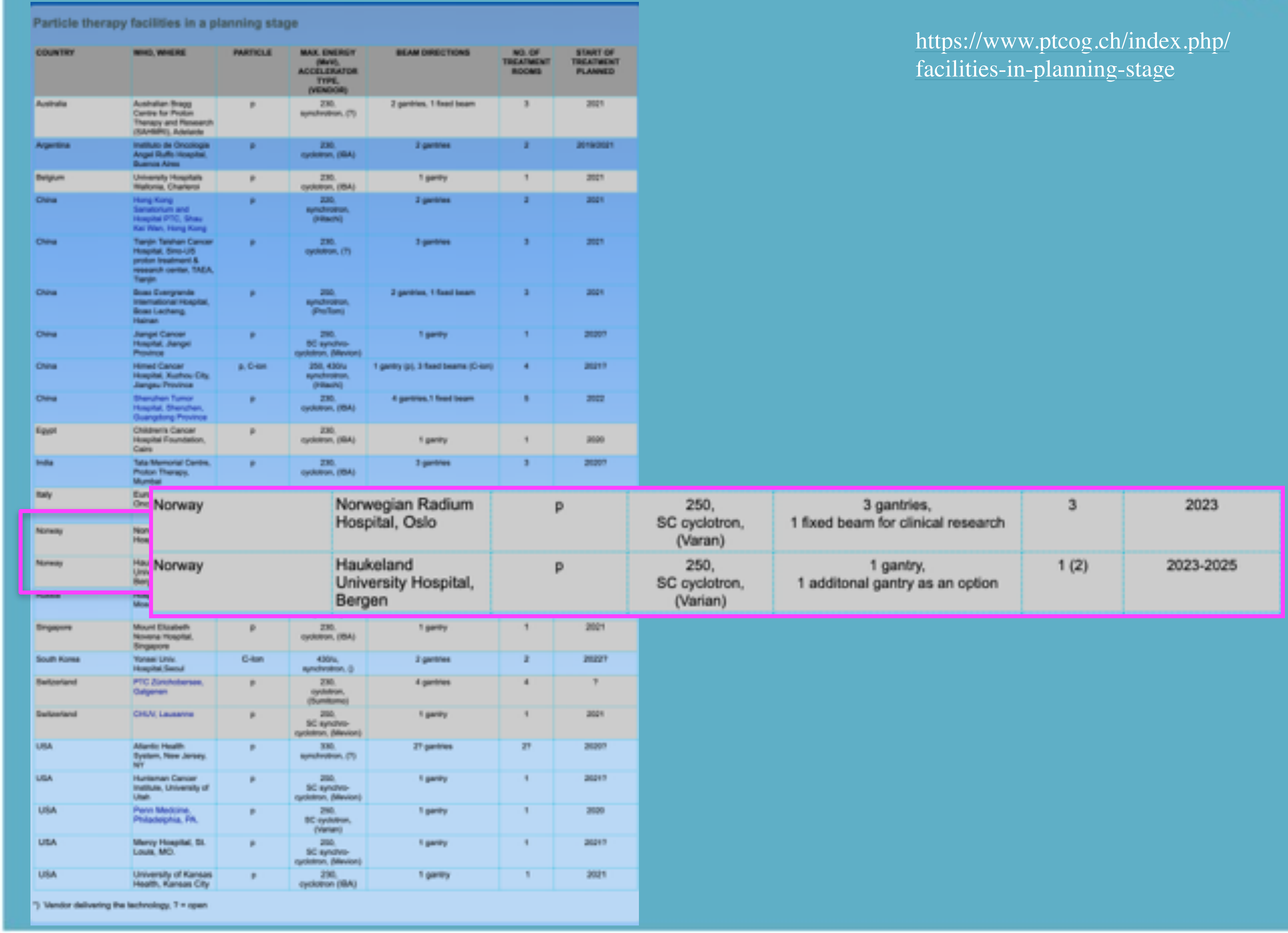

Particle therapy facilities in a planning stage

COUNTRY	WHO, WHERE	PARTICLE	MAX. ENERGY (MeV), ACCELERATOR TYPE, (VENDOR)	BEAM DIRECTIONS	NO. OF TREATMENT ROOMS	START OF TREATMENT PLANNED
Australia	Australian Bragg Centre for Proton Therapy and Research (SAHMRI), Adelaide	p	230, synchrotron, (?)	2 gantries, 1 fixed beam	3	2021
Argentina	Instituto de Oncologia Angel Roffo Hospital, Buenos Aires	p	230, cyclotron, (IBA)	2 gantries	2	2019/2021
Belgium	University Hospitals Wallonia, Charleroi	p	230, cyclotron, (IBA)	1 gantry	1	2021
China	Hong Kong Sanatorium and Hospital PTC, Shau Kei Wan, Hong Kong	p	220, synchrotron, (Hitachi)	2 gantries	2	2021
China	Tianjin Taishan Cancer Hospital, Sino-US proton treatment & research center, TAEA, Tianjin	p	230, cyclotron, (?)	3 gantries	3	2021
China	Boao Evergrande International Hospital, Boao Lecheng, Hainan	p	250, synchrotron, (ProTom)	2 gantries, 1 fixed beam	3	2021
China	Jiangxi Cancer Hospital, Jiangxi Province	p	250, SC synchro-cyclotron, (Mevion)	1 gantry	1	2020?
China	Himed Cancer Hospital, Xuzhou City, Jiangsu Province	p, C-ion	250, 430/u synchrotron, (Hitachi)	1 gantry (p), 3 fixed beams (C-ion)	4	2021?
China	Shenzhen Tumor Hospital, Shenzhen, Guangdong Province	p	230, cyclotron, (IBA)	4 gantries,1 fixed beam	5	2022
Egypt	Children's Cancer Hospital Foundation, Cairo	p	230, cyclotron, (IBA)	1 gantry	1	2020
India	Tata Memorial Centre, Proton Therapy, Mumbai	p	230, cyclotron, (IBA)	3 gantries	3	2020?
Italy						
Norway						
Norway						
Singapore	Mount Elizabeth Novena Hospital, Singapore	p	230, cyclotron, (IBA)	1 gantry	1	2021
South Korea	Yonsei Univ. Hospital,Seoul	C-ion	430/u, synchrotron, ()	2 gantries	2	2022?
Switzerland	PTC Zürichobersee, Galgenen	p	230, cyclotron, (Sumitomo)	4 gantries	4	?
Switzerland	CHUV, Lausanne	p	250, SC synchro-cyclotron, (Mevion)	1 gantry	1	2021
USA	Atlantic Health System, New Jersey, NY	p	330, synchrotron, (?)	2? gantries	2?	2020?
USA	Huntsman Cancer Institute, University of Utah	p	250, SC synchro-cyclotron, (Mevion)	1 gantry	1	2021?
USA	Penn Medicine, Philadelphia, PA.	p	250, SC cyclotron, (Varian)	1 gantry	1	2020
USA	Mercy Hospital, St. Louis, MO.	p	250, SC synchro-cyclotron, (Mevion)	1 gantry	1	2021?
USA	University of Kansas Health, Kansas City	p	230, cyclotron (IBA)	1 gantry	1	2021

*) Vendor delivering the technology, ? = open

Norway	Norwegian Radium Hospital, Oslo	p	250, SC cyclotron, (Varan)	3 gantries, 1 fixed beam for clinical research	3	2023
Norway	Haukeland University Hospital, Bergen	p	250, SC cyclotron, (Varian)	1 gantry, 1 additonal gantry as an option	1 (2)	2023-2025

Conclusions

- Proton therapy remains controversial, mainly because of its high cost relative to x-ray facilities
- The evident physics benefits expected in general have not been quantified and proven in large random trials, so a cost-benefit analysis is difficult
- The x-ray field is more more advanced, so a comparison with 'old fashioned' proton treatment, would be unfair, especially with modern IMRT irradiation modalities
- The modern IMPT modality not only allows proton therapy to be applied to tumors that could not be accessed before and allows better control of the dose distribution
- Randomized trials are now getting underway to make direct comparisons between IMRT and IMPT *(Frank S J, 2016)*
- The main problem is the so-called **'range problem'**

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To be continued …

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